



Science and technology networks in Scandinavia

The dominant science hubs in Scandinavia are akin to the open sandwiches favoured throughout the Nordic region — each country has its own name for, and unique approach to preparing, this delicacy. So, too, with science. Each hub has had different motivations and methods for building up local networks, as articles in this supplement reveal.

Finland invested in centres of excellence for research and development in response to an economic crisis. Stockholm and Uppsala relied on tradition for their base, and a new emphasis on mobility between academia and industry for growth. Medicon Valley was tied together after a bridge opened across the Øresund Sound in 2000, connecting Copenhagen and Malmö. And Norway is pumping oil revenues into research infrastructure, and must balance investment in traditional strengths, such as climate research and aquaculture, with attempts to improve its competitiveness in biomedicine.

But increasingly, scientific leaders in each of these areas are realizing that they cannot go it alone — even though each hub shows signs of expanding, both in terms of academic and industrial research. That realization is reflected across much of Europe. To compete with international juggernauts such as the United States, nations are realizing that they must pool their resources. The European Commission's Sixth Framework Programme for funding research, which came into effect last month, is designed to reward scientists who can build the most effective cross-border networks.

Doing so is especially important in Scandinavia, where the collective population — and research budget — is a fraction of those of Britain, France or Germany alone. Fortunately, the Nordic countries have already begun building what many refer to as 'a network of networks', which they hope will give them the competitive edge. The challenges they have faced and the lessons they have learned in beginning this process will undoubtedly inform scientists in other countries who are embarking on similar journeys.

Although Norway is the most recent Nordic country to start building networks, with the funding of a functional-genomics initiative and 13 centres of excellence this year, it is among the most active and innovative players, chairing the Nordic Council and planting the seed for one of the most sweeping pan-Scandinavian initiatives in the shape of MedCoast Scandinavia. *Nature* is pleased to acknowledge the financial support of Norway's Ministry of Education and Research in producing this supplement. As always, *Nature* carries sole responsibility for all of the editorial content.

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Building Nordic networks

Established bioregions across Scandinavia are increasingly joining forces in an effort to increase their international competitiveness. Paul Smaglik gets connected.

Taina Pihlajaniemi, director of Biocenter Oulu at the University of Oulu in Finland, travelled thousands of miles to a meeting on angiogenesis at Cold Spring Harbor Laboratory in New York this March — only to find herself having lunch with colleagues from neighbouring Sweden and Norway. Between courses, the conversation turned from the conference to each scientist's interest in extracellular matrixes. The meal ended with a predictable dessert. "We decided to combine our efforts and apply for European Union funding," Pihlajaniemi says. The three Scandinavian scientists have since gathered more European collaborators to seek funding from the European Commission's Sixth Framework Programme, which aims to award grants to researchers who set up cross-border networks in applied research.

Many other Scandinavian researchers find themselves in a similar situation, being driven together by varying degrees of serendipity, proximity and necessity. Of these, necessity is perhaps the dominant force. Norway, Denmark, Sweden and Finland are physically large, but they have small populations and limited resources. So over the past decade, each has built up research networks within its own borders in an effort to maximize what they have.



Taina Pihlajaniemi is building links for Oulu University.

More recently, the countries have turned their attention to their neighbours, seeking to create formal and informal connections with each other, and with nations beyond Scandinavia — particularly in the Baltic region.

FORCEFUL FRAMEWORK

The Sixth Framework Programme, which came into effect last month, is providing probably the largest incentive for this outbreak of cross-border networking. Ideally, it wants to inspire collaborations that involve several partners — and wealthier countries are encouraged to work with groups from less-developed regions. But this focus, along with the emphasis on applied research targeted at specific social outcomes, has drawn fire from many European researchers, who say that funding decisions should be made solely on the basis of the

quality of the science.

Pihlajaniemi sees both sides of the argument. On the plus side, she says, stimulating pan-European cooperation is positive. "It really forces scientists to try to work together," she says. But she is also concerned about the emphasis on research of social relevance and applied research. She says that she would prefer an emphasis on basic research that also fosters collaboration.

The Sixth Framework issues a challenge to scientists to build networks from the top down. But Scandinavian researchers are finding success by building networks from the bottom up — relying on informal collaborations as the basis for bigger endeavours. They are also cementing those extended relationships by having principals from one network sit on the boards of similar endeavours in a similar network in a neighbouring country.

These machinations are



necessary because networks require a large amount of time and effort from all the parties involved if they are to work. Without good communication and coordination, duplicated efforts can trump any benefit of interacting and waste any gains that might have resulted from sharing resources or infrastructure. And the broader and more far-flung the network, the greater the challenge.

A core element of one of the most ambitious pan-Scandinavian initiatives has informal origins. A loose coalition among Nordic resource centres for microarray production and analysis

UNIV. OULU

BIOCENTER OULU



SWEGENE: a spreading network for functional genomics.

emerged out of contacts made by Ola Myklebost, professor of biochemistry at the University of Oslo, and Åke Borg, an associate professor in the oncology department at Lund University, during their careers.

Both Borg and Myklebost were collaborating with a lab at the US National Institutes of Health that specialized in using microarrays for cancer research. That technology filtered through to Oslo and Lund when Myklebost met a Swedish contact at a microarray meeting run by the European Bioinformatics Institute. Myklebost was put in touch with Joakim Lundeberg at the Royal Institute of Technology in Stockholm as the central contact for microarray technology within the Wallenberg Consortium North (see page A19). He contacted Lundeberg and was, in turn,

Per Belfrage: establishing networks takes time.



contacted by Borg. The end result is an equal three-way partnership to generate a library of 30,000 complementary human DNA probes.

Now these ties are being strengthened by MedCoast Scandinavia, an initiative from several universities in Sweden and Norway that aims to harmonize efforts between Norway's FUGE and Sweden's SWEGENE functional-genomics programmes.

FORM AND FUNCTION

The Norwegian government started FUGE this year with an initial grant of 100 million kroner (US\$13.5 million), which is set to rise to 150 million kroner in 2003. SWEGENE, meanwhile, gets 60 million Swedish kronor (US\$6.6 million) a year, from the Knut and Alice Wallenberg Foundation, a Stockholm-based charitable organization that funds scientific research and education. Eventually, MedCoast hopes to collaborate with Medicon Valley, which helps to coordinate research activities in Lund, Malmö and Copenhagen (see pages A24 and A27).

One of the challenges faced by MedCoast is the fact that the programmes are at different stages of development. FUGE is just starting up, whereas SWEGENE began in 2000. In fact, the Wallenberg Foundation is likely to stop funding SWEGENE in 2005, with the expectation that the government will take over once



Growth industry: Scandinavia seeks strength in research.

the infrastructure is built.

Meanwhile, another putative player, the Biotech Research and Innovation Center (BRIC), Denmark's equivalent of FUGE and SWEGENE, is barely off the drawing board. After years of discussion, plans for a 27,000-square-metre research facility that BRIC will share with the University of Copenhagen and the Copenhagen Hospital Corporation have only just been approved. But once the initiative is up and running, it is expected to join MedCoast.

Per Belfrage, chairman of the Biomedical Center at Lund University and a member of SWEGENE's board, sympathizes with the difficulties involved in trying to integrate several projects on different schedules. "It takes a long time," he says.

A very personal kind of networking is needed to smooth those considerations, says Claus Braestrup, an executive vice-president at Copenhagen-based drug firm Lundbeck, and chairman of BRIC. To foster ties with the Swedish shore of MedCoast, he also sits on SWEGENE's board and anticipates that scientists in both projects will share resources.

Collaborations between several countries are even easier

when the emphasis is on fostering links with researchers exploring the same questions from different angles rather than on sharing data in formal repositories. That is why Morten Overgaard, a graduate student in the department of psychology at the University of Aarhus in Denmark, formed the Nordic Network for Consciousness Studies two years ago. It allows him to interact with, say, a Finnish philosopher on issues of introspection and first-order consciousness.

Although in this Internet age proximity seems less of a concern, it still has its advantages, and it emphasizes the informal nature on which the network was founded. "We have easy mobility for people to visit each other's labs without much planning or expense," says Overgaard.

The need to share infrastructure may be driving the Nordic nations together, but the demand for personnel is making some scientists look to the Baltic. Leaders of several Scandinavian networks last year formed ScanBalt, which aims to increase mobility for scientists between Scandinavia and neighbouring countries such as Poland, Latvia, Estonia, Lithuania and western Russia,



Finn-Medi Centre part of Finland's fresh impetus in R&D.

especially St Petersburg.

Børge Diderichsen, a vice-president at Danish drug firm Novo Nordisk in Bagsværd and vice-chairman of ScanBalt, predicts that over the next four years there will be a shortage of potentially hundreds of scientists, given the growth of biotechnology in Denmark alone. "It is very likely there will be a labour shortage — particularly among skilled scientists," he says.

Diderichsen notes that the

Baltic countries have a tradition of good training in many of what he calls the "traditional skills" in the hard sciences — mathematics, physics and chemistry. Those skills are in demand in much of the Western world, with fewer students taking courses in chemistry in Britain and the United States, for example, and Scandinavia is no exception.

At the same time, Baltic countries lack some modern facilities such as the proteomics

and structural-biology centres now being developed in Scandinavia by FUGE and SWEGENE. ScanBalt would ideally match the two. "We can make some of the infrastructure and some of the advanced research equipment available to researchers in the east," says Diderichsen.

The tricky part will be promoting a flow of talent to Scandinavia without exploiting it. "We are opposed to any notion of a brain drain in the Baltic regions," he says. Instead, he would like to see a circulation of talent. One way to do that would be to create a ScanBalt University in the Baltics, perhaps in Poland, which could be staffed by scientists from both regions.

BROAD CONNECTIONS

Another initiative has already begun making similar arrangements, but on a smaller scale. Mart Saarma, director of the Institute of Biotechnology at the University of Helsinki, is originally from Estonia, and wants to establish ties between his new country of residence and his homeland.

He is trying to arrange a twin-city science project between Helsinki and Tallinn in Estonia. Apart from Saarma's heritage, two factors make the project potentially viable — proximity (the cities are 1.5 hours apart by ferry and about 20 minutes by helicopter) and politics (Estonia is set to join the European Union in 2004).

But the same factors that have driven other hubs in Scandinavia to network also come into play here. Joining together in research ventures will make the twin cities more scientifically competitive. And combining commercial forces should do the same economically, Saarma hopes.

Within the past few years, Scandinavia has begun to extend its networks beyond the Baltics to the United States, the United Kingdom and the Far East. For example, the University of Oslo this year set up a research agreement in biomedicine with Johns Hopkins University in

Baltimore, Maryland. And in October, the Swedish Consulate initiated a joint biotechnology venture fund with California (see "On the road to California", page A9).

In Finland, the University of Kuopio is actively seeking international partners. A delegation recently returned from Minnesota, where it reactivated an agreement to exchange students, researchers and teachers between Kuopio and the University of Minnesota.

Such free exchange of research is benefiting all of the scientists involved. When, in 1996, Howy Jacobs left the United Kingdom for a post at the Institute of Medical Technology at the University of Tampere, he was more enamoured with Finland's commitment to science funding (see "Finnish envy", left) than he was with the idea of building collaborations — but that was the end result.

Jacobs, a self-described "refugee from the British funding crisis of the early 1990s", stayed in touch with two UK groups, one at the University of Cambridge studying how metazoan mitochondrial DNA replicates, and the other at the University of Glasgow studying the genetics of fruitflies. He has since established a scheme to place Glasgow undergraduates in his Finland lab for 10 months.

His work is part of a project that has been designated as a centre of excellence by the Academy of Finland. Known as FinMIT (the Finnish research unit on mitochondrial biogenesis and disease), the project has helped Jacobs to build strong links throughout the Nordic region. He interacts with fellow FinMIT researchers at the University of Helsinki, and he also works with Nils-Göran Larsson at the Karolinska Institute.

Jacobs' happy landing illustrates how necessity, proximity and serendipity can lead to productive research interactions. And it also shows that building on informal ties can help to sustain them.

Paul Smaglik is editor of *Naturejobs*.

Finnish envy

Finland has a history of exporting much of its scientific talent. Many members of the faculty at the Karolinska Institute in Stockholm are Finnish, for example. So why are scientists in Scandinavia currently looking at Finland with green eyes? The simple answer is money.

Until the 1990s, Finland's infrastructure was relatively underdeveloped. But after a recession in the 1980s, the government invested heavily in science and technology in an attempt to transform the economy. As a result, Finland's budget for research and development (R&D) rose from 2.3% of its gross domestic product (GDP) in 1994 to almost 3.4% in 2000.

"They have really pushed," says Hans Wigzell, president of

the Karolinska Institute, who sees Finland's plans as a way to rally the Swedish government to increase funding for basic rather than applied research.

Norwegian scientists are especially galvanized by Finland's example. Although they are pleased that the government is funding 13 centres of excellence, many say privately that its aim to raise R&D investment from 1.7% of GDP to 2.2% by 2005 is not sufficiently ambitious.

If other countries don't step up their funding, top researchers may head to Finland. "We are now starting to get Swedish researchers in Finland, which was very uncommon 10 years ago," says Kalervo Väänänen, director of the anatomy department at the University of Turku.

P.S.

On the road to California

Sweden and California are separated by 7,000 miles and a large polar ice cap, but that is not standing in the way of a budding partnership in biotechnology. In October, the Swedish consulate in Los Angeles announced a programme to aid and expand academic and industrial ties between California, a giant in biotechnology, and Sweden, which is positioning itself as an emerging global leader.

At a seminar held by the consulate in October, Consul-General Andreas Ekman announced that a major aim of the programme is to “establish a joint Scandinavian–Californian biotechnology venture fund to support advanced biotech research commercialization”. Proposed by the office of the governor of California, Gray Davis, the fund is intended to provide a cushion for venture capitalists. Ways of financing it are currently being investigated, but officials at the governor’s office say that they hope new companies can be seeded by combining investments from pension funds, Swedish and Californian venture-capital companies and research institutes.

With so many top-notch academic and industrial research institutions in California, why should Californian investors turn to Sweden? Alexander Suh of California Technology Ventures, an

early-stage venture-capital firm in Pasadena, says that foreign investors are attracted by the Swedes’ high level of education, mastery of English, commitment to funding social aims, and their strong tradition of supporting scientific research.

Through the Nobel prizes, they have come to be seen as the “arbiters of science in the world”, in the words of David Baltimore, president of the California Institute of Technology. And a strong research infrastructure certainly exists in Sweden. In addition to a long tradition of excellence in academic research, medical and technical universities are developing collaborations based on new technology platforms combined with clinical trials taking place within the medical universities.

Unfortunately, the void left by the departure of large pharmaceutical companies from Sweden represents a major gap in the revenue streams needed for funding the later stages of biotech product development. Anders Flodström, president of the Royal Institute of Technology in Stockholm, says that for Swedish biotechnology to succeed, the research base needs to be expanded dramatically, and business models need to be developed that encourage significant reinvestment in university and company infrastructure.

ATTRACTIVE PROSPECT

A major factor in attracting venture capital to Sweden may turn out to be its intellectual property laws, which entitle professors to ownership of inventions developed within academic systems. Flodström points out that the major disadvantage of this system is the lack of reinvestment in research infrastructure that would come out of licensing such inventions, which could create an unsustainable system.

Suh argues that to the contrary, it is professors’ ownership of intellectual property that makes Sweden so attractive to foreign investors, who see negotiations with universities that hold rights to inventions as an impediment to investors. He cautions that Sweden should not necessarily emulate business models developed in California if it wants to stimulate foreign investment.

More generally, there are major differences between US and Swedish culture that might affect investment. Whereas Americans are quite used to having no safety net, risk-taking is not

so prevalent in European culture. Moreover, the strong labour laws in Europe represent another downside to investing in European companies. But opportunities for Swedish investment are certainly abundant and needed.

Flodström notes that for biotechnology to succeed in Sweden, the Swedes need to expand their research base dramatically by attracting big grants to fill the void left by the departure of the large drug companies. He stresses that the appropriate business models should be chosen in the initial stages of investment, and technologies that bear products in a short timeframe, such as bioengineering and medical devices, should be developed as a stronghold, saying that they will be much more important in the short term than proteomics and gene sequencing.

STEM-CELL SUPPORT

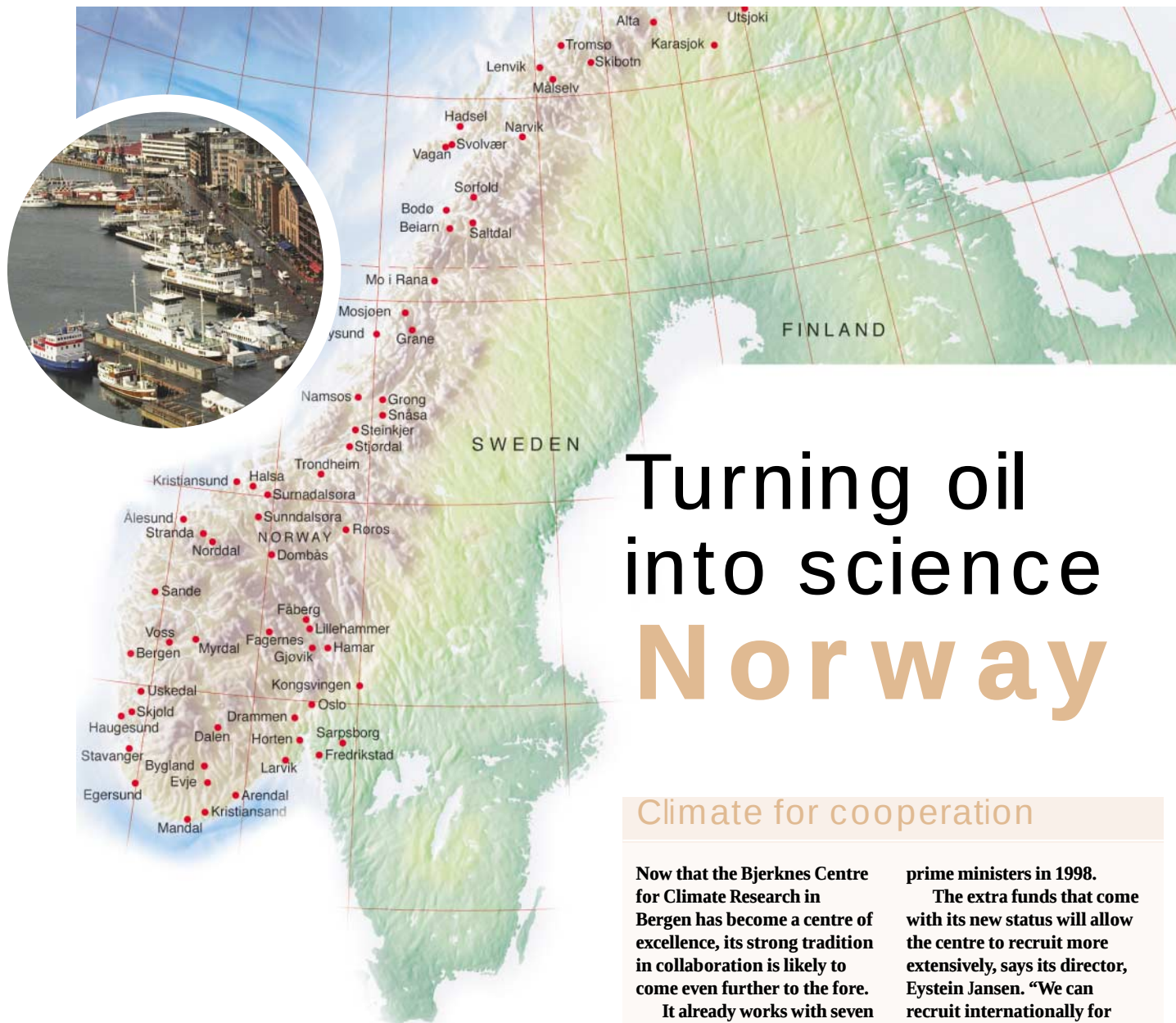
Although it is a long-term prospect for investors, stem-cell research has nonetheless emerged as a field where Sweden can develop natural synergies with US research institutes. When President Bush announced the US policy restricting embryonic stem-cell research using funds from the National Institutes of Health (NIH) to only those cell lines existing as of that date, it turned out that 24 of those lines were held by the Karolinska Institute and Gothenburg University.

Recently, Governor Davis signalled support of stem-cell research in California by signing a bill that authorized stem-cell research from any source, including embryonic stem cells, as long as it was approved by an institutional review board. Flodström predicts that scientists in Sweden are gearing up towards a major push in embryonic stem-cell research, which should begin within a year, once funding is in place, and that major scientific collaborations will emerge between US and Swedish universities, probably funded by the NIH. It is likely that technologies will grow around handling of the cells, and this in itself could lead to new areas of business.

The consulate’s programme also features an ongoing seminar series on areas of biotechnology in which Sweden provides leadership, such as proteomics, immunology and neurobiology, as well as banquets to celebrate California’s Nobel laureates, and has helped delegations of journalists and venture capitalists to visit Sweden.

Natalie DeWitt is a senior biology editor at *Nature*.





Turning oil into science Norway

Climate for cooperation

Now that the Bjerknes Centre for Climate Research in Bergen has become a centre of excellence, its strong tradition in collaboration is likely to come even further to the fore.

It already works with seven other Norwegian centres and over 60 institutes across 14 countries. Many of its projects have sprung from these collaborations. For example, the Norwegian Ocean Climate Project, a UK–Norwegian initiative on abrupt climate change, was originally proposed by the countries’

prime ministers in 1998.

The extra funds that come with its new status will allow the centre to recruit more extensively, says its director, Eystein Jansen. “We can recruit internationally for young scientists to enhance our talent.”

He expects to take on up to ten postdocs and five graduate students as a result. The funds will also allow the centre to bring in more scientists for temporary stays.

P.S.
Bjerknes Centre for Climate Research
♦ www.bjerknes.uib.no

Norwegian research institutions have historically tried to temper potential international recruits’ perceptions about the country’s cold, dark winters with talk of its natural beauty and excellent skiing. That approach has not been entirely successful — there are usually more Norwegian scientists leaving than foreign ones arriving. But the new government elected last autumn is planning a different tack.

“I think it’s wrong to try to attract researchers with the fjords and the mountains,”

says education and research minister Kristin Clemet. “We need to attract them with good research opportunities and afterwards we can tell them about all the other things.”

To create those opportunities, the country is providing the missing ingredient — money. Norway lags far behind its neighbours Sweden — which spends three times as much per capita on biomedical research — and Denmark, which spends twice as much. At 1.7% of gross domestic product (GDP), Norway’s investment in research and development is well below the average of 2.2%

quoted by the Organisation for Economic Co-operation and Development (OECD).

Norway has started to close that gap by tapping into something it has plenty of, at least in the short term — oil. Oil revenues were used to set up the Research Investment Fund in 1999, as a source of extra funding for science. Clemet

hopes that the fund, plus incentives for university researchers to commercialize their work and tax credits to promote industrial investment, will bring Norway’s scientific funding in line with its neighbours, and boost R&D up to or above the OECD average.

The fund, at 13 billion kroner (US\$1.7 billion), is ahead

Fishing for partners

Ever since Bjørn Høyheim, a scientist at the Norwegian School of Veterinary Science in Oslo, switched from pigs to fish, he has had better luck trawling for partners and casting for cash. He first received funding in 1997 to be a coordinator for SALMAP, a consortium funded by the European Commission (EC) to generate genetic maps of the Atlantic salmon, rainbow trout and brown trout. The group consisted of scientists from Norway, Denmark, Scotland, Ireland, France and Canada. Many of the same players then got EC funding for SALGENE, which aimed to build an

expressed sequence tag database for salmon.

So far Høyheim says that he has found it relatively simple to coordinate activities with his Norwegian partners in Oslo, Bergen and Trondheim.

But relationships beyond the borders are a bit trickier. For example, working with a microarray facility in Scotland can be difficult, because competition inevitably mixes in with cooperation, he says. But when resources for each country are dwarfed by those of, say, the United States, it is the only real option. "It doesn't make sense that all of us should develop the same tools," says Høyheim. **P.S.**

of schedule to meet its 15-billion kroner target for 2005. The current year is pivotal for science in Norway, as it marks the 525-million kroner yield's first investments, including 100 million kroner for a functional-genomics initiative and 70 million kroner to establish 13 centres of excellence.

A government white paper recommends that at least one centre be awarded in each of four broad categories — marine research; the intersection between energy and the environment; medicine and health; and information technology. But the centres awarded so far are tilted more

heavily towards the first two, which are areas in which Norway already has an established research tradition or has infrastructure in place.

For example, the Bjerknes Centre for Climate Research in Bergen recently became a centre of excellence. A joint-research venture, it already has plenty of collaborations set up within and beyond Norway (see "Climate for cooperation", page A13).

Other centres named tended to support existing industries within Norway, such as aquaculture, ships and ocean structures, and petroleum research. Only one centre dedicated to biomedicine was funded in the first round — the Centre for Molecular Biology and Neuroscience at the University of Oslo.

FUGE STATE

In some respects, FUGE, the functional-genomics project, is serving as a test case for how well Norway can scale up its science. Clemet likes it because it combines marine, biotech and environmental science. And to succeed, the programme will require both contact with international partners — such as Canada, which is working with Norway to sequence the salmon genome — and

industry, which is looking at the science behind many aspects of salmon raising (see "Fishing for partners", left).

"We want to be the leader in the world of salmon genomics," says Lars Aukrust, a member of the Research Council of Norway. But he thinks that will require more leadership from the government — he and the scientists who proposed FUGE had hoped that the first year of the project would be funded at three times the rate. "There is no sense of urgency," Aukrust says of the government.

But Ole Marvik, chairman of the Norwegian Bioindustry Association, says that the country does not yet have enough infrastructure to absorb a bigger boost. "You cannot create 500 trained people overnight even if you had the money," he says. He notes that the Norwegian biotech industry, with what he calls 45 "true" companies — about half of which are less than three years old — could not sustain excessively rapid growth.

Despite the modest starting size of FUGE and the centres, the two programmes will clearly have an impact on recruitment and employment, says Marvik, with a few hundred positions created immediately, and more commercial spin-offs and academic-industrial collaborations to follow. Although the money is not massive compared with the sums bandied about in the United States, it is enough to encourage more cooperation within Norway and to foster international collaborations. "The amount of money spent is not an important thing alone," Marvik says. "What's important is how this investment is creating a momentum."

Although Werner Christie, chairman of Norway's Biotechnology Advisory Board, agrees with Aukrust that the rate of investment should be increased, he thinks that the first rounds of both programmes have given the country enough momentum. "I think we will catch up," he says.

But that will require more than just a sustained investment,



Ole Petter Ottersen: hopes to encourage biomedical collaborations.

says Christie, who spent 1999–2001 in San Francisco learning the mechanisms of the bay area's biotech base. There he witnessed "the power of beer and pizza", the fuel that drives networking in the United States. "We have to learn that in Norway," he says.

Establishing FUGE and the centres of excellence will play a key role in forming Norway's part of that broader bioregion. "In FUGE, we see a new principle in Norwegian research strategy — the universities joining forces to launch a coherent research programme based on a national sharing of technology and resources," says Ole Petter Ottersen, who runs the Centre for Molecular Biology and Neuroscience. But the government must commit to raising the overall R&D budget every year, he adds. Proposals to increase funding for FUGE to 150 million kroner and to boost basic research overall by 600 million kroner will help. "With the growing importance of regional and international collaborations, and the increasing mobility within Europe and between continents, it would be detrimental to Norwegian research, should we remain as an underachiever in R&D spending," Ottersen says. ■

Paul Smaglik is editor of *Naturejobs*.

FUGE www.forskningsradet.no/fag/andre/fuge

Research Council of Norway

www.forskningsradet.no/english
Bioindustry Association

www.biotechforum.no

This article is an updated version of a feature published in *Naturejobs* on 2 May 2002.

Kristin Clemet: emphasizing science over fjords and mountains.



Blurred vision

Seeking to capitalize on Sweden's scientific strengths, Stockholm and Uppsala are bringing business and academia together, says Paul Smaglik.

Sweden, it seems, has a major case of role reversal. In Stockholm, the head of pharmaceutical company AstraZeneca's global drug-discovery unit hails from the Karolinska Institute. By contrast, the leader of the Karolinska Institute's genome and bioinformatics centre once worked for Astra.

In Uppsala, the situation is similar. There, scientists and executives at Amersham Biosciences, the life-sciences equipment firm, often teach at Uppsala University, and professors at the university are becoming increasingly involved in local start-up firms, which themselves are often run by managers who developed their skills at Amersham.

Such movements and connections were unheard of in Sweden 10 years ago, but now they are increasingly common. They represent a blurring of the boundaries between commerce and academia that has come about through both necessity and design.

On the one hand, the failure of the Swedish government to increase its commitment over the past decade to basic biomedical research as aggressively as the United States or Finland, has forced academics and industrialists to forge connections. But at the same time, scientists in both sectors have realized that in order to

compete internationally, they need to create larger research networks.

STOCKHOLM STRATEGY

One of the key architects of Sweden's new public-private culture in science is Hans Wigzell, who became president of the Karolinska Institute in 1995. In recent years, Wigzell, who is also a science adviser to the Swedish government, has set up Karolinska Innovations to handle technology transfer from the institute, and has also created the Karolinska Fund to provide venture-capital investment.

In addition, in 2000 he helped to establish Actar, a drug-development company based in Stockholm. Actar is designed to help university researchers from across Sweden to exploit any potential drug

Hans Wigzell is seeking links with commerce.



Stockholm: home to a range of public-private initiatives.

targets that they identify. And earlier this year Wigzell bought shares in the Scandinavian Clinical Research Institute, a contract research organization that helps small companies to conduct clinical trials.

When Wigzell first arrived at the Karolinska Institute, he encountered some resistance to such commercial ties. But he counters such criticism, saying that commercial interactions not only provide non-governmental funds for basic science, but also help to translate basic science into cures for disease. "I think it is unethical for a modern medical school not to support in every way the means to turn its research into practical application," Wigzell says.

Sweden has the highest number of biotech firms per capita in the world — partly because government-funded university scientists are allowed to own all of their intellectual property (see page A9). But this policy may also be limiting the size of these companies, as individual scientists often do not have the resources to grow their firms beyond the scale of small start-ups. This drawback may well be countered by the sheer number of companies in Sweden, which should allow firms to join forces and grow. "We have a great opportunity to link things together," says Wigzell.

To a greater extent, that potential remains to be realized. Unlike the links that

are being established between Sweden and Denmark, in which the Medicon Valley Academy coordinates activities among companies and the universities in Lund, Malmö and Copenhagen (see pages A24 and A27), northern Sweden has relied on ad hoc personal networking. But that is changing.

GETTING CONNECTED

The Knut and Alice Wallenberg Foundation, a charitable organization based in Stockholm that promotes scientific research and education in Sweden, is starting to take a leading role by setting up and funding initiatives such as the functional-genomics network known as the Wallenberg Consortium North (see “North and South”, below). Similarly, the Swedish Foundation for Strategic Research, which supports work in the natural sciences, engineering and medicine, is funding local efforts such as the Stockholm Bioinformatics Center, but it is now looking beyond Sweden (see “Swedish fund branches out”, right).

Plans are also being hatched to bring things more closely together at the Karolinska Institute. Wigzell's most ambitious scheme is to turn a disused railway yard in the shadows of the Karolinska campus into a science park, with the help of Stockholm University and the Royal Institute of Technology (KTH) also in Stockholm. He refers to the space, which is close to all three research institutions, as “gold”.

Commercial thinking at the institute is not limited to Wigzell's construction aspirations. Since his arrival, for example, Wigzell has made professors at the Karolinska compete for their internal grants, and he has upped the mix of adjunct professors to 61 — a quarter of the total at present — to ensure that students get to interact with faculty members who have one foot in industry or government work.

Jan Lundberg, global head of research and development for AstraZeneca, has taken such interaction one step further. In 1995, he joined the Stockholm-based drug company after

Swedish fund branches out

The Swedish Foundation for Strategic Research, originally established in 1993 to support research in natural science, engineering and medicine, is now spending some of its capital outside the country. In one collaboration with the Academy of Finland, the foundation is supporting bilateral projects under the heading ‘Microbes and Man’. The programme will fund joint research projects

between Finnish and Swedish researchers studying host–microbe interaction.

The foundation now disperses 1 billion Swedish kronor (US\$110 million) a year to researchers, but will reduce that amount to 650 million kronor in 2005 until the fund runs out in 2020. P.S.

The Swedish Foundation for Strategic Research

► www.stratresearch.se/index.htm

18 years as a professor of pharmacology at the Karolinska Institute. The move, he says, has allowed him to continue working with his ex-colleagues.

AstraZeneca has over 100 university collaborations with Swedish researchers, ranging from funding basic research to testing compounds in animal models for disease, the majority of which are with the Karolinska. “There is a history here,” Lundberg says. “People know each other. If they get a new idea, they come to us first.” But the balance is delicate. “We don't have the same mind-set and the same goals,” says Lundberg.

big biotech,” says Lundberg.

But outside money is necessary, argues Claes Wahlestedt, director of the Karolinska's Center for Genomics and Bioinformatics, because national resources have not kept pace with need. Wahlestedt, who left AstraZeneca for the medical centre after five years at the company's site in Montreal, Canada, says that the Karolinska's research budget has kept growing because private funding has increased faster than public funding over the past few years.

Per-Åke Nygren, a biochemist at the KTH's institute for astronomy, physics and biotechnology, agrees that private funds are necessary to maintain basic research. Groups from his lab spun off technology that helped to lead to the creation of companies such as Pyrosequencing in Uppsala, Affibody in Bromma and Creative Peptides Sweden in Stockholm. Those companies have all sponsored research at the KTH at some point, he says.

But Nygren admits that depending too much on this type of funding can be dangerous. For example, in October, Pyrosequencing was forced to cut 25 positions from its headquarters.

UPPSALA INSTRUMENTAL

If AstraZeneca and the Karolinska create a gravitational pull towards Stockholm, then Amersham Biosciences and Uppsala

North and south

The Knut and Alice Wallenberg Foundation, which funds scientific fellowships, research equipment and infrastructure, has in recent years turned to configuring two functional-genomics networks. In 2000, the foundation started SWEGENE in the southwest and the Wallenberg Consortium North. The development of the two illustrates the difficulty inherent in such projects.

SWEGENE, the smaller, more centralized of the two, took off much faster than its northern counterpart, says Erna Möller, executive director of the foundation. “It's probably more difficult to have a bigger network,” he says. The three southeastern institutions in SWEGENE will

receive 60 million Swedish kronor (US\$6.8 million) a year for five years, whereas the seven central and northern institutions of the Wallenberg Consortium will get 100 million kronor over the same time period.

Characteristic of other organizations in Sweden, there is “substantial interaction” between the two networks, Möller says. Möller's own background is indicative of Swedish mobility between sectors and institutions — the former Karolinska Institute researcher still has an active research group there and also sits on AstraZeneca's board of directors. P.S.

Wallenberg Consortium North

► wcn.ntech.se

SWEGENE

► www.swegene.org

University have a similar effect on the Uppsala region. But the past five years have seen some uneven trends. On the one hand, employment in the company has risen by 30% since 1997, when Pharmacia Biotech merged with UK-based Amersham Life Sciences.

But after the merger, several employees left to form their own start-ups. Initially, Per-Erik Sandlund, Amersham's global vice-president for operations, was concerned about these departures, but he has since changed his tune. "It's a very positive thing," he says. "We've got to work harder in order to keep our employees within the company."

One way to keep people is by collaborating with academic initiatives. For example, Amersham supplies proteomics instrumentation to some members of the Wallenberg Consortium North and the functional-genomics programme, SWEGENE, based at Lund University in the south.

Such collaborations allow the company to improve its instrumentation by learning about what sorts of scientific goals the universities are pursuing and what sort of obstacles they are finding, says Lars Hagel, director of external research and development at Amersham, and an associate

professor of analytical chemistry at Uppsala University.

His ties have also benefited Uppsala University. Together, the company and the university created a medical mass-spectrometry lab, which Amersham uses to improve its machines' diagnostic capabilities. The company is also working to promote protein science by giving out an award, co-sponsored with the Royal Swedish Academy of Sciences, to a young Swedish researcher conducting work in the field.

SPUN-OFF SUCCESS

Many of the spin-offs in Uppsala result from technologies that Amersham found were best suited for exploitation outside the company. Gyros is a prime example. This company aims to use microfluidic channels etched onto the surface of compact discs to conduct biochemical assays. When Amersham scientists developed the technology, "they had no clue as to what they were going to do with it," says Maris Hartmanis, president and chief executive of Gyros. Now the company's investors resemble a 'Who's Who' of Scandinavian science — Amersham and AstraZeneca have shares, as do venture-capital firms HealthCap in Stockholm and BankInvest in Copenhagen. The Knut and Alice Wallenberg Foundation also holds a significant stake.

Research interactions are important to QUIAtech, a firm in Uppsala whose core technology purifies and amplifies oligonucleotides for microarrays. Marek Kwiatkowski, the company's chief scientific officer, is also an associate professor in biorganic chemistry at Uppsala University and the company is housed in a science park on campus. Kwiatkowski, who splits his time between the company's office and his university lab, says that the borders between the two are becoming increasingly blurred, a fact that, much like Wigzell,



Gyros has benefited from Uppsala's positive climate.

he believes can only be beneficial.

Bengt Westermark, professor of genetics and pathology at Uppsala University, is not sure that this is entirely a good thing. When he was a young investigator, he was "quite suspicious" of collaborating with any company, big or small, he says. Although he admits that he has loosened up in recent years, his concern is that such collaborations will emphasize applied research to the exclusion of more basic work.

Westermark, who will head the Swedish Cancer Society in Stockholm next year, is also concerned that the government will not address the fundamental structural problem that may be driving more people to rely on private money. He says that, overall, grants are too small and end up "fragmented" among too many investigators. He is also suspicious of enforced networks, such as the European Commission's Sixth Framework Programme for research funding, that emphasize large networks of collaborators.

"If you dictate a network, then I fear that within the network there will be groups that are less competitive than others — and some groups will be excluded because of personal relationships or whatever," Westermark says.

His most favoured solution is also the most unlikely — larger project grants akin to those provided by the US National Institutes of Health, which would amply fund a lead

investigator, several postdocs and graduate students. Such grants would increase the element of university research that he most values — academic freedom. "If you are wrong, you just change direction," Westermark says.

TOWARDS PARTNERSHIP

More public money — especially for basic rather than applied research — would benefit both the public and private sectors, and mean that academic research universities would no longer need to rely on companies so much, say Lundberg and Wigzell. But few would disagree that the alliances so far created have been largely positive.

Wigzell adds that the increase in funding that has come from companies has allowed some institutions — and even cities — to put aside petty differences. For example, Amersham's impact on bolstering proteomics and instrumentation in Uppsala and AstraZeneca's ties to the Karolinska Institute in drug discovery and development have helped each city to carve out its own identity.

That, in turn, has diminished the rivalry between the two, which are only separated by an hour's train ride. "Uppsala has always felt like the little brother," Wigzell says. But now the two are increasingly looked on as partners in one region, rather than rivals in two. "We are making it together," Wigzell says.

Paul Smaglik is editor of *Naturejobs*.

Marek Kwiatkowski splits his time between industry and academia.



MEDICON VALLEY



Bridging sectors

Medicon Valley

A bridge spanning the Øresund Sound now connects biotech companies in southern Sweden and northern Denmark. Associations with local universities tie the companies to the area, and a plethora of venture capital funds fuel them. But for Medicon Valley's growing body of biotech companies to take off, they need one more resource that is in increasingly short supply — scientists.

"The bottleneck used to be venture capital," says Anker Lundemose, chief executive of Pantheco, a Danish biotech company. "The bottleneck now is human resources." About 2,000 R&D employees work in the region's 95 companies. But the growth in both new companies and venture funds means that more scientists will be needed.

The area must attract more talent from beyond what has traditionally been a fairly insular community, say area bankers, biotech executives and university administrators.

And it will also need to retain the best and brightest PhDs produced by the concentration of universities that created the Medicon Valley Academy — the organization that basically organized the region's biotech into one operational unit (see *Nature* **395**, 412–413; 1999).

Claus Bræstrup, executive vice-president, R&D, of Lundbeck, the Copenhagen-based pharmaceutical firm, says companies will need to look outward more but successful overtures to researchers in other countries may not be easy. "There are major obstacles for people coming in to Denmark," Bræstrup says. "One is the taxes; another is the weather."

Denmark has already begun to address the tax system, which levies rates as high as 62% for the best-paid scientists. Last year, it established an 'expert' bracket, which allows out-of-country workers with skills in demand to pay only 25% for three years.

The country had a similar programme before, but it only applied to the highest-paid

Beyond the valley

In Odense, Denmark, biotechnology is becoming a way of life. In a recent inventory to seek out areas of economic growth, the local government identified 15 biotech companies and 22 medical technical firms, in addition to the area's academic institutions.

The government has since dubbed the region BioTEAM South and hopes that improved organization will help the area to build on earlier successes, such as the University of Southern Denmark's work relating to the recently sequenced genome of the malaria parasite

***Plasmodium falciparum*. Matthias Mann, a bioinformatician at the university, worked with researchers from the Netherlands and the Sanger Institute near Cambridge, UK, to analyse the parasite's proteome.**

Scientists in the region now hope to build on that success through the university's Centre for Proteome Analysis in Life Sciences. The area is also positioning itself for more international collaboration by joining the ScanBalt initiative (see page A3).

P.S.
BioTEAM South
www.bioteam.org

positions — and anyone deciding to stay on after three years was required to pay back the difference. More people are eligible under the new system, and the assimilation penalty no longer applies. But the tax break can cause resentment among co-workers who pay the higher rates, Bræstrup says.

Lundbeck has recruited extensively outside the country — adding 117 R&D workers in the past year and doubling its research budget in the past two. The company is especially short on organic chemists and bioinformatics experts.

Kirsten Drejer, chief executive of Symphogen, a



Pointing the finger: Pantheco chief executive Anker Lundemose pinpoints the shortage of scientists as the major bottleneck to biotech growth.



Cold comfort: the long, dark Scandinavian winter can act as a deterrent to scientists coming from warmer regions, according to some industry experts.



Independent streak: Lund University's Eva Degerman fears that reliance on industry funds will reduce academic freedom.

Danish biotech company specializing in developing human antibodies to viruses, says she is having an especially hard time finding senior people. She agrees with Bræstrup that the Scandinavian weather — especially the long, dark winter — can make it hard to recruit scientists from warm sunny regions such as California. “On the other hand, it's very safe,” says Søren Mouritsen, chief executive of M&E Biotech, one of the first Danish biotech companies. He tries to emphasize to recruits that the area is considered to offer excellent quality of life.

RETAINING TALENT

Meanwhile, some scientists who were trained in the area are reluctant to whole-heartedly embrace industry. “The public researcher is still a little bit shy about collaborating with private investors,” says Hans Poulsen, chief executive of Odin Medical, a Copenhagen-based company that is developing nonviral gene-therapy vectors to fight cancer.

Poulsen has combated that cultural tendency by making his company into a bit of a hybrid. It is supported in part by the Danish Cancer Institute and is housed on the University of Copenhagen campus. Poulsen also expects his employees to do basic research and publish their findings. As a result of this approach, he has been

successful in finding qualified candidates. It is important to offer a research setting in a non-academic environment, because academic slots have been increasingly scarce due to a dearth of government funding, Poulsen says.

Eva Degerman, from Lund University's section for molecular signalling, is concerned about a similar trend in Sweden, which is especially pronounced in Stockholm and Uppsala (see page A19). She would prefer not to have to rely on industry to fund her research. “I think it is important that we have our independence,” she explains.

But that may become increasingly difficult. Degerman, like many Swedish scientists, depends on government and foundation money to support her work. These funds have not been rising nearly as fast as they have in the United States, and she is worried that too much dependence on industry money will result in less freedom to publish and an over-emphasis on product over basic research.

Per Belfrage, former dean of Lund's medical school, thinks that Medicon Valley-area academic scientists who learn to interact with the region's industry can help themselves retain their independence.

For example, if industrial and academic scientists band together under the aegis of the Medicon Valley Academy, they may be able to lobby successfully for more basic biomedical funding — something scientists from both sectors say is lacking. Although the government cannot control the climate, it can do something about funding. ■

Paul Smaglik is Naturejobs editor.

Medicon Valley Academy

♦ www.mva.org

Copenhagen Capacity

♦ www.copcap.com

This article is an updated version of a feature published in Naturejobs on 21 June 2001.

A commercial angle

The Institute of Experimental and Clinical Research at Denmark's University of Aarhus is fashioning itself into a miniature version of Sweden's Karolinska Institute, according to its director Jens Christian Djurhuus. It is doing this by emphasizing commercialization and industrial interaction, says Djurhuus, who is also president of the Danish Medical Research Council, a government advisory body.

But while the Karolinska Institute focuses much of its university-industry relations on drug discovery and

development, institutions at Aarhus are geared towards biomedical monitoring. Interactions between the Aarhus University Hospital and the Institute of Experimental Clinical Research bears this out. For example, the two are now collaborating on ways to monitor *in vivo* physiology using a host of technologies.

As a result, about 20 members of the institute now have their own companies, and many split their time between their commercial interests, independent research and, in some cases, medicine. For example, Torben Ørntoft,

whose company AROS Applied Biotechnology is designing diagnostic chips for cancer, is also a professor with the institute and employed by the hospital as a senior doctor.

Djurhuus welcomes such developments, but says that the downside is the possibility of less academic interaction. Danish science is “fragile” because of the relatively low level of public funding, Djurhuus says. Too much commercial work could disrupt the dialogue that exists between scientists receiving public and private funding, he adds. P.S.

Biotechnology in the Medicon Valley

Although the Øresund bridge now links southern Sweden and Denmark, it will take a while to establish good working relations between their biotechnology clusters. Lone Frank reports.

Medicon Valley — a bi-national 'bioregion' spanning greater Copenhagen in Denmark and Skåne in southern Sweden — has set itself the ambitious goal of becoming Europe's most attractive bioregion by 2005. And that goal might, indeed, be feasible as the movers and shakers in the international biotechnology community eye this expanding cluster with interest. With one of the fastest growth rates, in number of start-ups, in Europe, the Medicon Valley may indeed become a leader in Europe if it can successfully integrate the two regions.

BIOTECH IN THE VALLEY

The Medicon Valley concept debuted during 1993, when a report from urban geographers Christian Wichmann Matthiessen and Åke Andersson highlighted the potential of life sciences within the region. In particular, the report pointed out that Medicon Valley is home to 60% of Scandinavian pharmaceutical companies and is ranked third in Europe on the basis of number of medical publications by researchers in the region. Indeed, Medicon Valley can boast 135,000 students, 26 hospitals, and 11 universities, including the large Copenhagen and Lund Universities.

The message got through to the Øresundscomiteen, a forum

of counties from both regions hoping to drive development in the region. In particular, the forum chose to promote biotechnology, coining the term Medicon Valley in 1994 and later helping to set up the networking organization Medicon Valley Academy (MVA) to spur development and to assist knowledge transfer between universities and the private sector. The MVA now has a substantial presence in the area, with offices in both Denmark and Sweden. It arranges regional meetings and conferences, and has recently started setting up educational programmes and stipends for postgraduate students working within biotechnology.

The pharmaceutical

industry has been a presence in Medicon Valley for decades. Southern Sweden is home to major corporations including Pharmacia and AstraZeneca, whereas Novo Nordisk, Lundbeck, Ferrosan and Ferring are located in Denmark. Biotechnology in the valley first arose in southern Sweden, where it sprang out of university research in the form of companies such as BioInvent and Biora during the 1980s. In Denmark, the industry made its debut slightly later with the creation of NeuroSearch, established in 1989 by a group of researchers from Novo Nordisk and Ferrosan. NeuroSearch develops drugs to treat diseases of the central nervous system, and now has

The new Øresund bridge connects southern Sweden and Denmark.



F. DEAN/GETTY IMAGES





WONDERFUL COPENHAGEN CVB

a market capitalization of about US\$100 million, making it the third-largest biotechnology entity within Denmark today. To some extent, NeuroSearch served as a psychological battering ram for the biotechnology sector in the valley, demonstrating to the cautious Danish business community that it was possible to build a company with no imminent profits and a significant cash-burn rate. The company also became a breeding ground for biotechnology executives, and many of its former employees now occupy key positions in other companies.

Today, the valley's commercial centre of gravity remains firmly on the Danish side, where the density of start-ups is much greater. There are 32 biotechnology companies in Sweden and 80 in Denmark (see Table 1 for examples). MVA director Bent Christensen credits the difference to the "big city effect" — the draw of Copenhagen and its efficient infrastructure. The Swedes, however, are gearing up: the year 2001 became the first in which the number of biotechnology start-ups on the Swedish side equalled those in Denmark — each registered six. According to some Danish observers, entrepreneurial spirit is more pronounced in Sweden, where academics are more willing to risk leaving university posts for start-ups. Gertrud Bohlin Ottosson, director of the Ideon science park in Lund, disagrees, suggesting other

reasons for the Swedish growth spurt: "Since the late 1980s our biotech industry was overshadowed by information technology, which was the main focus with investors," she says. Since the worldwide dot-com bubble burst, venture capital has been rerouted to biotechnology. And, at the same time, the large Swedish pharmaceutical companies are concentrating on core competencies, outsourcing more work to biotechnology start-ups.

FOREIGN INTEREST

Things have moved fast since the humble beginnings of the Scandinavian biotechnology sector. Today, with over 100 biotechnology companies in a region of only three million inhabitants, Medicon Valley has one of the highest densities of companies per capita in Europe.

Just six years ago, venture capital dedicated to biotechnology was unknown in Scandinavia. Today, however, a host of local and foreign

investors have earmarked \$650 million for biotechnology. Lately, Medicon Valley has managed to attract significant interest from abroad. The first to dip its toes in the water was Californian company Maxygen (Redwood City), which moved in three years ago to acquire the then one-year-old Danish company Profound with the help of Danish investment bank BankInvest. Since then, the operation in Hørsholm, north of Copenhagen, has grown from a handful of employees to nearly a hundred.

Last spring, the local media applauded loudly when US major-league player Biogen decided to place a new biomanufacturing facility in Hillerød, north of Copenhagen. The plant, which will employ 400 people and bring in \$35 million in investment, is scheduled to open in 2005. "I believe that this decision firmly put Medicon Valley on the map and that it will help bring in more investment," says MVA's Christensen. Before the announcement, there was a

Table 1: Selected biomedical companies in the Medicon Valley

Denmark

Acadia Pharmaceuticals	Genomics-based drug discovery
ALK Abelló	Allergy treatments: R&D and production
Bavarian Nordic Research Institute	Gene therapy and vaccines
Biolmage	System for detecting intracellular signal transduction
Combio	Gene-based drug discovery
Exiqon	Microarray and high-throughput solutions for genetic profiling and gene-expression analysis
Genmab	Development of human monoclonal antibodies for treatment of chronic disease
Maxygen	Protein-based pharmaceuticals, developed through structure-based analysis and robotic screening of candidate molecules
NeuroSearch	Novel therapeutics for neurological and psychiatric disorders
NsGene	Genetically engineered neuronal cell cultures for gene-based treatments of CNS disorders, such as Parkinson's and Alzheimer's disease
Pantheco	Peptide nucleic acid-based antibiotics for treating drug-resistant pathogens
Pharmexa	Therapeutic vaccines for the treatment of chronic disease
Symphogen	Recombinant human polyclonal antibodies
7TM Pharma	Drug design focused on G-protein-coupled receptors

Sweden

Active Biotech	Pharmaceuticals and vaccines based on immunobiology
Biolinvent International	Specific antibody fragments for research tools and therapeutics
Biora	Development of oral therapeutics to treat periodontal disease and improve healing after oral surgery
Cellavision	Image analysis, software and hardware for improved diagnosis

14-month race in which several European bioregions were assessed as possible future homes for the plant. According to James C. Mullen, Biogen's chief executive officer (CEO), the quality of the workforce and the area's "world class in biotechnology and pharmaceuticals" weighed in favour of Medicon Valley.

MAKING A MARK

However, the unrivalled star of Medicon Valley, Genmab, is the result of a successful collaboration between locals and outside players, and observers are hopeful that it is a sign of deals to come. In the year 2000, US-based Medarex and BankInvest set up the antibody company Genmab in Copenhagen as a joint venture. By October of that year, Genmab, making the most of the opportunity afforded by the upsurge in market interest in biotechnology, had one of the most successful European initial public offerings to date, raising \$220 million.

Genmab, whose main asset is an exclusive licence to Medarex's HuMab technology, develops human antibodies directed against targets related to cancer and various autoimmune diseases. Today, the company has a market capitalization of \$500 million, placing it securely as the area's largest biotechnology operation; the second-largest company, allergy drug developer ALK-Abelló, is just a third of Medarex's size.

The location of Genmab in Medicon Valley is key, according to Genmab's CEO Lisa Drakeman. "The availability of venture capital and access to skilled clinicians and patients to help conduct clinical studies are essential," she says. Medicon Valley also has several other advantages: the public health system is practically a monopoly, with record keeping tied to a personal identification number given to everyone at birth. Furthermore, in general, Scandinavians are more willing than most to participate in clinical trials, making trials

very cost-effective.

Now, comfortably past the venture funding stage, Genmab has been able to continue building alliances with foreign companies, among them deCODE Genetics (Reykjavík, Iceland) and Gemini Genomics, now owned by Sequenom (San Diego, California). Although among the youngest, Genmab is the only Medicon Valley company to have a product in phase III clinical trials — the tumour-necrosis factor- α (TNF- α)-inhibiting antibody HuMax-CD4, for the treatment of rheumatoid arthritis. Some say that the company has set a new standard for professionalism and ambition, especially in raising venture capital funding. "While the American way is to raise all the capital you can while the window is open, a Danish CEO would typically be more modest and only go for the amount he thinks he needs," says BankInvest director Jesper Zeuthen.

MATURE FUNDING

To date, the development of biotechnology within Medicon Valley has benefited less from government investment in

biotechnology business than some other regions; government initiatives have been focused on building excellence at the basic research level rather than providing "soft money" for start-ups. However, start-ups can receive financial backing from the Swedish Industrial Development Fund and Danish Business Development Fund, which are networked with the MVA. Biotechnology ventures can find shelter in the five science parks — Symbion, Hørsholm and CAT in Copenhagen, Ideon in Lund, and Medeon in Malmö — which are supported by a mix of private and public funding. Mostly, biotechnology in Medicon Valley has evolved under its own steam, and the current situation looks set to continue, despite arguments in favour of more government support. Indeed, Asger Aamund, an angel investor and chairman of the board of NeuroSearch and several other companies, has for years complained that the government has not provided tax breaks on stock options and warrants in order to motivate more academic researchers to make the jump into business. Fortunately, however,

Big city effect: Copenhagen's efficient infrastructure has proved to be a draw to biotech firms.



WONDERFUL COPENHAGEN CVB

Scandinavian venture capital is now more seasoned and prolific. The pioneer was Copenhagen's BankInvest, which set up the area's first specialist biotechnology fund during 1997. Since then, BankInvest has expanded to create two more funds, and a host of other local funds such as Novo Capital and Medicon Valley Capital have been established. Today, there are about 32 investors in the region.

What is perhaps most important is that the region's capital base is fast becoming international. "The ability to draw international investors will be a staple for the companies who survive in the future," says Florian Schönharting. The man behind the BankInvest biotechnology funds for ten years, Schönharting has now moved on to co-found and direct Denmark's youngest biotech venture-capital company, Nordic Biotech. Schönharting and his partner, Christian Hansen, are currently raising their second round of funds and are looking for outside partners. As one of the area's few specialized early-stage funds, Nordic Biotech has so far managed to attract investment from California's Biotechnology Value Fund and related investors.

Meanwhile, well-known heavyweights such as Swiss Index Ventures, Alta Partners, Apax and Lombard Odier have moved into the area, investing in companies such as 7TM Pharma, Genmab and BioImage. Swiss Index's director Francesco de Rubertis has even named Medicon Valley the preferred location for future investments by his fund. This February, Finland's largest life-science venture fund, BioFund, set up an operation in Copenhagen as its first step into Europe. BioFund director Seppo Mäkinen says that Medicon Valley is clearly the area with the greatest potential within Scandinavia, and Schönharting agrees: "The period 2000–01 has been a breakthrough year and the outside interest shows that Medicon Valley has now attained critical mass."

It remains unclear as yet whether there is enough high-quality, innovative research to invest in within Medicon Valley. BankInvest's Zeuthen is worried that the well of innovative projects could start to run dry in a few years, although Schönharting points out that the deal flow has actually been increasing over the past few years. But at the same time, Schönharting stresses the need to look outside Scandinavia and import ideas and technology from other regions.

TROUBLES AHEAD

And there could be more snakes in paradise: the difficulty of recruiting suitably qualified personnel could stunt the future development of biotechnology in Medicon Valley. Several biotechnology players have long argued that there will be a shortage of qualified researchers for the biotechnology industry because universities in Denmark and Sweden are pumping out too few life-science graduates. Per Salholt, research director of Novozymes — formerly part of Novo Nordisk — says that although he is still able to recruit the necessary staff, he worries about the future. "As all the new start-ups grow, there will be a serious demand, and the output from universities does not match the [expected] need in just three or four years," he says. As an indicator, the number of biotech employees in Denmark and Sweden grew by 30%, to 3,500, during 2001.

At the Copenhagen start-up 7TM Pharma, management has had to recruit the entire staff of its chemical department from outside Scandinavia, because of the shortage of postdoctoral chemists at home. According to chief operating officer Peter Moldt: "It is possible to lure researchers to Scandinavia, but it demands a lot of time and effort and that takes a toll on small operations." On the positive side, stresses Moldt, although it may be difficult to attract researchers from academia, mobility among researchers in big pharmaceutical companies has increased dramatically

as the biotechnology sector has matured.

Meanwhile, unusual initiatives are cooking in the academic world. One is the DanSing programme, which Medicon Valley universities are taking on a road show to Singapore this spring. The institutions are negotiating for the opportunity to educate 1,000 Singaporean life-science graduates in Medicon Valley over five years. The hope is that some of these students — recruited from the top 5% of students in Singapore — will stay on in the region to feed the hungry biotechnology industry.

"Being an attractive bioregion ultimately comes down to one thing — excellent research," says Per Belfrage, chairman of MVA and a professor at Lund University. Although Denmark may be leading the commercial race so far, Sweden is further advanced in boosting the academic arena. Sweden also benefits from a few wealthy private research charities such as the Wallenberg Foundation, which has helped to create the \$80-million SWEGENE initiative, which supports a high-profile institution for postgenomic research. Public money backed the \$120-million Biomedical Center launched in Lund during 2000, which is already planning to expand.

Meanwhile, the Danes are shaking their heads because the counterpart to the Biomedical Center in Copenhagen, the Biotech Research and Innovation Centre (BRIC), remains stuck on the drawing board. Danes complain that their politicians act too slowly and do not appreciate the need

for speed within the sector.

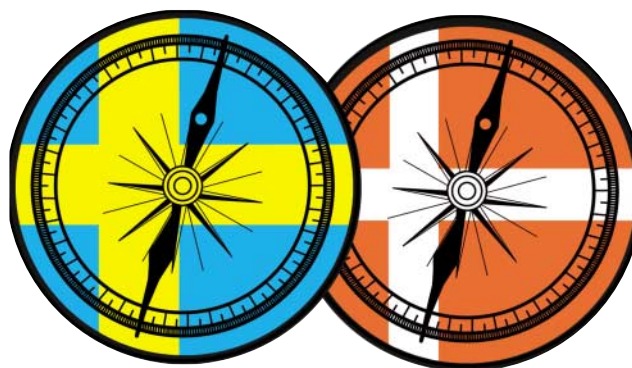
Claus Bræstrup, BRIC chairman and research director at Lundbeck, regards the Biomedical Center as a wonderful initiative but believes that the planned opening in 2004 is the very last call. "Politicians must give stronger support to research if the region is to ultimately succeed," he says.

Succeeding as a region also means bringing two cultures together, which poses structural problems for Medicon Valley. Although the two-year-old Øresund Bridge provides a physical link between Copenhagen and Malmö, integration is far from complete. Forming collaborations between the two countries remains a challenge, and there is still a feeling that Medicon Valley is more a theoretical construction than a reality. According to Ideon's Gertrud Bohlin Ottosson, the practical problems loom large: students are deterred from crossing the bridge because of the costly toll (\$60), whereas companies complain that the different tax systems deter employees from commuting from one side to the other to work. But the most detrimental omission is the paucity of collaborations across the region, says Bohlin Ottosson. "It will take time to get this aspect going, and the only way is to keep on pushing, to arrange more meetings and conferences and to keep discussing the need to further integrate the region."

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This article first appeared in *Nature Biotechnology* (20, 433–435; 2002).



Finnish biotechnology — built on solid foundations

Committed investment in research infrastructure has laid the foundations for a vibrant biotechnology community in Finland, says Riku Lähteenmäki.

Although perhaps better known for its fish, forests and mobile phones, Finland has a substantial presence in biotechnology. The sector has evolved naturally out of a well-established biomedical research base, which has been supported by generous and committed public and private financing. Today, aided by local venture capital, at least five biotechnology clusters have sprung up around Finland. Although the industry is young and predominantly privately owned, this chilly North European country offers a warm hearth for biotechnology start-ups.

REVIVING THE ECONOMY

Finland is poor in natural resources such as oil, gas and coal, and in the past most of its wealth has come from metal production and machine making, as well as forestry and its associated industries. As a result of a combination of local and global factors — including the demise of the Soviet Union, a key export destination — the Finnish economy went into a nosedive during the 1980s, and the government recognized the need to build a more modern industrial base. As a result, the



At the hub: Biomedicum Helsinki houses, entirely or in part, six of Finland's Centres of Excellence.

government and local industry jointly supported programmes designed to raise the level of technological know-how in Finland, and biotechnology and information technology were top priorities.

The Finnish government has remained committed to this cause, generously supporting research and development (R&D). In 2001, R&D spending was about 3.4% of gross domestic product (GDP), a total of €4.4 billion (US\$3.87 billion) — the second highest (after Sweden) percentage GDP of any country in the world. About 30% of this investment comes from the public sector and 70% from the private sector.

Finland also benefits from a receptive climate for biotechnology — most of the country's five million inhabitants have a positive attitude towards technological advances. Companies such as Nokia, the world's leading manufacturer of mobile phones, have set a precedent, demonstrating the potential for



Genes in Helsinki

The Centre of Excellence in Disease Genetics, coordinated by the National Public Health Institute, takes advantage of the unique characteristics of the Finnish population — its geographical isolation, small founding population and excellent healthcare system. The centre hopes to understand the genetics of diseases of the central nervous system, and to identify the genetic component of diseases common in Finland, such as multiple sclerosis, colon cancer and asthma. The Centre of Excellence in Disease Genetics is the largest of the 11 centres focused on biological sciences. All the research is carried out within the Biomedicum Helsinki building, located on the

campus of the University of Helsinki next to the University Hospital. Opened in 2001, Biomedicum Helsinki provides a first-class international medical research and training environment, with state-of-the-art facilities for 1,000 researchers and students. The building also hosts, entirely or partially, six Centres of Excellence, several units of the Faculty of Medicine, the Finnish Genome Centre, and various support services. Biomedicum's director Olli Jänne says that although the primary function of the centre is to facilitate basic research and training, it will help to generate a number of companies. Indeed, a business incubator in the vicinity of Biomedicum is being planned.

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rapid growth by Finland's high-technology sector.

Today, there are over 120 biotechnology companies (including service businesses) in Finland, ranking the country sixth in Europe after the United Kingdom, Germany, France, the Netherlands and Sweden. Finland's strategy is to concentrate on areas in which it has a strong research base — pharmaceuticals, diagnostics, biomaterials, functional foods and enzymes.

DRIVE FOR HIGH-TECH

The rapid rise of Finland's technology sector can be traced back to the national technology programmes put in place by the government during the 1980s. The National Technology Agency (Tekes) was established in 1983 to coordinate these programmes, which subsequently became the main channels for public funding of technological R&D in Finland. Tekes operates under the government's Ministry of Trade and Industry and is staffed by 240 industry experts. Tekes' annual budget is about €390 million — roughly 30% of the total public R&D expenditure in Finland — of which a third is channelled into life-science research.

Tekes, companies, research institutes, and in some instances the Academy of Finland, jointly plan the technology programmes, which helps to generate cooperation and networking between academia and industry. Each programme typically lasts three to six years, is carried out by several research groups in separate locations, and consists of tens of publicly and privately financed projects. To get funding, companies and research institutions must file project applications with Tekes, which provides 50–60% of the total costs.

NeoBio, one of the many biomedical programmes, specifically funds biomedical projects with the vision of supporting the development of biotechnology platform technologies and, ultimately, the creation of businesses able to compete internationally.

Launched in October 2001, NeoBio has approved 32 projects, funding them with a total of €50 million. According to programme coordinator Riikka Heikinheimo, applications from industry are accepted slightly more often than those from academia. NeoBio has a total of 53 projects, when the 11 old Tekes projects and the 10 run by the Ministry of Agriculture and Forestry are included. Projects encompass agricultural biotechnology, industrial biotechnology and cell-based biomanufacturing. Thirteen of the projects are carried out in companies and 40 in research institutions. All the projects are carried out in Finland, but Tekes provides an additional contribution for headhunting

top-level researchers from abroad. Heikinheimo says that it is crucial for projects to involve foreign researchers to ensure that they achieve international standards.

Tekes actively encourages the commercialization of innovations resulting from the projects it funds. Applicants are asked whether they have found a partner to which to transfer their technology, or plan to found a business using the intellectual property. If a start-up company is planned, Tekes will investigate the project's commercial potential. If the project is deemed viable, Tekes and the Finnish National Fund for Research and Development (Sitra) provide funding through a joint programme called LIKSA, designed to help

commercialize innovative projects. Up to €35,000 is given to help the researchers write a formal business plan using the services of a local technology transfer company. To date, LIKSA has financed four business plans within NeoBio.

However, the most significant impact of NeoBio on the Finnish economy in coming years will probably be the generation of intellectual property rather than large numbers of start-ups. Heikinheimo says: "We do not expect readily commercializable products from the programme, but it will develop know-how and technologies that can be used in product development at a later stage, and every project should yield at least one patent."

In addition to Tekes, ► A39

Table 1: Selected biomedical companies in Finland

Company	Focus (Region)
Drug discovery	
Ark Therapeutics	Gene-based products to treat cardiovascular disease and cancers (Kuopio)
BioTie Therapies	Dependence disorders, inflammation, glycobiology (Turku)
FibroGen Europe	Recombinant human collagen and gelatin (Oulu)
Finncovery	Drug modelling, prodrugs, cyclodextrins (Kuopio)
FIT Biotech	DNA vaccines and gene therapies (Tampere)
Galilaeus	Cancer-drug development and manufacture (Turku)
Hormos Medical	Hormonal agents to prevent and treat age-related diseases (Turku)
Juvantia Pharma	Therapies for psychiatric, neurological and vascular diseases (Turku)
MAP Medical	Radiopharmaceuticals for treating cancer (Kuopio)
Diagnostics	
Biofons	Diagnostics for intestinal inflammatory and autoimmune diseases (Turku)
Bio-Nobile	<i>In vitro</i> toxicity assays, luminescent biosensors for environmental monitoring (Turku)
Erilab	Antibodies, analytical services, <i>in vitro</i> diagnostic tests (Kuopio)
HyTest	Monoclonal antibodies, proteins and enzymes (Turku)
InnoTrac Diagnostics	Immunoassay reagents, research reagents (Turku)
Jurilab	DNA chips for diagnostics and drug targeting (Kuopio)
Labmaster	Immunoassays and PCR reagents, enzymes, antibodies (Turku)
Medix Biochemica	Monoclonal antibodies, immunoassays and other chemistry kits (Helsinki)
Nanobac	Immunoassay reagents and kits for detection of nanobacteria (Kuopio)
SBA Sciences	Diagnostic kits for osteoporosis and bone-metabolism research (Oulu)
Biomaterials	
Bionx Implants	Bioabsorbable implants for surgical use (Tampere)
StickTech	Glass-fibre reinforcement technology (Turku)
Vivoxid	Bioactive glass for oral, facial and orthopaedic applications (Turku)
Enzymes	
Finnzymes	Thermostable DNA polymerases for PCR, enzymes for molecular biology (Helsinki)
Genencor	Industrial enzymes and special biochemicals (Other)
Roal	Industrial enzymes for food, feed, textile and pulp applications (Other)
Functional foods	
Aromtech	Ingredients for functional foods and cosmetics (Other)
Novatreat	Immunologically active milk products (Turku)
Omecol	Cholesterol-lowering products (Helsinki)

Finland's biotechnology clusters

HELSINKI

The University of Helsinki is the largest in Finland and has a long tradition of research in the natural sciences, in particular cancer biology, molecular neuroscience, plant molecular biology and structural virology. The university is now the epicentre of a burgeoning biotech cluster.

In 1995, a new Biocenter building was built just outside the city to facilitate biomedical research. Next to the Biocenter buildings is a 4,000-square-metre business incubator administrated by the Helsinki Science Park, and a new 13,000-square-metre incubator building is under construction. "We had four companies in the science park in 1996, and there are now 40. Thirty of them originated from the University of Helsinki," says a senior official at the science park. The companies employ about 300 people, and there are 2,000 researchers and technical staff in neighbouring institutions. According to the official, the incubator buildings are owned by both public institutions and private investors. Helsinki Science Park also provides assistance in patenting and licensing, business management, international marketing, finance and training in entrepreneurship. There is an emphasis on education about the development of good manufacturing processes (GMP) and good laboratory processes (GLP) laboratory-quality systems for researchers commercializing biotechnology innovations.

TAMPERE

Biotechnology in the Tampere region is concentrated in the Finn-Medi Technology Centre, which encompasses the Faculty of Medicine of Tampere University, the Institute of Medical Technology (IMT), biomedical research units of the Technical Research Centre of Finland, the Clinical Trial Centre and several other medical research and education institutions.

More than 1,000 of the 12,000 people who work in the Finn-Medi Technology Centre specialize in biotechnology and medical technology. The technology centre has facilitated the launch of about 40 health-technology and biotechnology companies, including Bionx Implants and FIT Biotech. Tampere's strength has been to combine different biomedical disciplines to develop, for example, novel bioactive implants, says Matti Eskola, managing director of Finn-Medi Research.

Eskola expects new biomaterials companies to emerge in the near future.

On the Finn-Medi site, an 8,000-square-metre premises is under construction, with private investors' money, in addition to the existing 25,000-square-metre science park. Other plans for the development of Finn-Medi include establishing a hospital for fitting prostheses, a tissue bank, a laboratory for motion research and a centre for tissue engineering. In 2001, IMT, Tampere University of Technology and the Faculty of Medicine jointly launched a new master of sciences programme in biomedical research and biotechnology, which focuses on bioinformatics and tissue engineering.

KUOPIO

The development of the Kuopio region arose out of the University of Kuopio's expertise in human health and the environment. Research at the A. I. Virtanen Institute — named after Artturi Virtanen, who won a Nobel prize for his animal-fodder preservation technology — has gained worldwide recognition in the fields of animal and plant biotechnology, molecular medicine, neurosciences, drug design and food biotechnology.

When healthcare technology is included, the Kuopio region can boast of 58 life-science companies, employing 850 people out of the 3,000 in the region working in biomedical fields.

The Teknia high-technology buildings provide 55,000 square metres of space, of which 20,000 square metres are dedicated to biotechnology and house companies, research units and a state-of-the-art biotechnology production unit with GMP-grade animal cell and microbial bioreactor laboratories. Mediteknia is a new 8,000-square-metre research centre, which will be financed mainly by the government, the European Union and the city of Kuopio at a cost of €14 million. It will comprise a Drug Research and Development Centre, a Clinical Research Centre, and a Food and Health Research Centre. Mediteknia is projected to increase collaboration between the university drug-research groups and the pharmaceutical industry and to transfer new products and technologies to the private sector. Kuopio's objective is to combine R&D on human health, nutrition and the environment, covering the entire food chain from 'farm to fork', as well as the drug-development process from target identification to clinical research.

OULU

Founded in 1986, Biocenter Oulu was Finland's first biotechnology research institute. The Biocenter is a virtual organization, networking the bioscience, medicine and process-technology faculties of the University of Oulu. Biocenter Oulu has been used as a model unit for the Finnish Centre of Excellence Programme, and has spun out more than ten biotech companies, many originating from local collagen research. The city of Oulu has invested about €10 million in a pilot manufacturing plant built to GMP standards, which allows researchers to move research into production. Next to the pilot factory is Oulu University Hospital, and the Medipolis incubator building, currently hosting some 40 companies. In addition, a joint programme called BioOulu, run by the electronics and biotech units of the Technical Research Centre of Finland and the University of Oulu, is about to establish a biosensor research unit in Oulu. The unit is one of the spearhead projects of Bioforum, founded this year by local players such as the Biocenter, to improve collaboration inside the biocluster and between different technology sectors.

TURKU

About half of Finland's pharmaceutical and diagnostics companies are located in Turku, and around 300 patented inventions in pharmaceuticals and diagnostics have originated from the Turku region. The BioTurku community consists of three universities, a polytechnic, some 30 biotechnology companies, and more than 600 bioscience researchers. The BioCity and PharmaCity buildings, which are located close to the university campuses and the Turku University Hospital, have a total 55,000 square metres of floor space and house, in addition to the biotechnology companies, the Centre for Biotechnology, Centre for Biomaterials, the pharmaceutical biotechnology unit of the Technical Research Centre of Finland, the Functional Foods Forum, a business incubator and other service organizations. According to Tapio Hurme, manager of the incubator, the aim is to launch 50 new biotechnology companies by the year 2010. The city of Turku has invested €14 million and has zoned 113,000 square metres to permit the construction of biotechnology production facilities in the nearby Turku BioValley area.

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► the Academy of Finland implements public financing of innovation in the country. The academy's goal is to improve the quality and reputation of basic research in Finland to maintain a competitive pipeline of innovations that can be commercialized in the future.

BUILDING ON BASICS

The academy receives €160 million in annual funding — about 12% of total public R&D spending in Finland. Life sciences received €40 million funding during 1999, and funding has been growing at about 20–30% per year for the past three years. About 85% of the academy's funding is directed to academic research. For example, the Life 2000 programme, financed to the tune of €14 million during 2000–03, consists of 89 research teams working on a total of 39 projects in neuroscience, developmental biology, functional genomics, biophysics, bioinformatics, and the ethical, legal and sociocultural aspects of bioscience research. Tekes is involved in the planning of the programme and finances two of the projects.

Programme coordinator Mika Tirronen says that the programme is a response by the academy to the needs of Finland's life-science sector. Tirronen says that initiatives for a programme come from the grass roots — from academic and industrial researchers — and those science council members responsible for planning the programme are active researchers themselves. Individual projects for a programme are selected on a competitive basis with the help of tens of Finnish and foreign experts, who give statements on applications.

The Academy of Finland also runs a Centres of Excellence programme designed to develop creative research and training environments by supporting the development of multidisciplinary research units that can become internationally

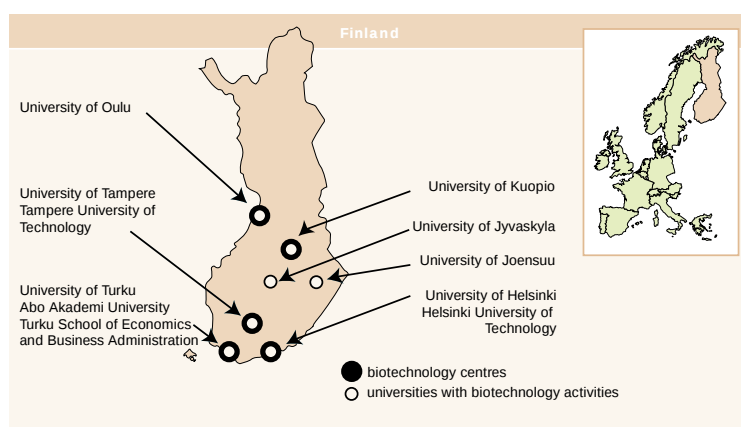
competitive. Eleven of the 26 Centres of Excellence nominated by the academy are biotechnology-related (see "Genes in Helsinki", page A35). The units have an average of 50 staff members apiece and work on a variety of projects, including research into cell-surface receptors, the genetics of disease, collagen, forest biotechnology, cancer biology, structural virology, biomaterials and tissue engineering. Funding for the centres comes not only from the academy but also from universities, research institutes, Tekes, government ministries, companies and foundations.

For the past eight years, the government has also invested heavily in regional development, in part through the Centres of Expertise programme. Whereas the Centres of Excellence programme funds research regardless of its location, the Centres of Expertise programme seeks to create a favourable infrastructure for business on a regional level, providing infrastructure and services to enable commercialization of research innovations.

TEAMING UP

One function of the programme is to generate team spirit within the regions, promote regional strengths, and thereby improve companies' competitiveness. Industry, local governments, universities, polytechnics, research institutes and other branches of public administration in each region are brought together to decide on future investments. Five regions are active in biotechnology — Helsinki, Turku, Tampere, Kuopio and Oulu (see "Finland's biotechnology clusters", page A37). Local technology centres run the programme, which receives a total annual funding of €200 million from the national government and local players including government, companies, universities and other investors.

Finnish biotechnology has clearly benefited from a



generous support of its basic-research infrastructure by the government, the European Union, and private foundations and companies, but researchers continue to experience problems in translating success at the bench into viable business opportunities. In particular, academic researchers have difficulty raising funding for the very early stages of starting up a company. To ease this process, Tekes provides up to €13,000 for market research about a potential invention — information essential for a winning business plan — in addition to the aforementioned LIKSA grants available for writing business plans.

Another problem is the shortage of skilled management, in particular managers experienced in product development and business strategy within life sciences. With only a limited local pharmaceutical industry, Finland may have trouble filling posts with qualified professionals. Fortunately, at least for now, the supply of graduates is meeting the needs of the industry.

Almost all start-up funding for biotechnology companies in Finland comes from venture capital. About 95% of venture capital comes from domestic companies, predominantly BioFund and Sitra, although many smaller local venture-capital funds exist. Although BioFund now invests internationally, it has a portfolio of €180 million, half of which is invested in Finland. Sitra, a venture-capital organization working under the mandate of

the Finnish parliament, invests €70 million in financing Finnish biotechnology start-ups.

But Matti Eskola of the technology centre Finn-Medi Research says that the financing of the commercialization process should be more streamlined, so that pre-seed, seed and venture capital are available for a starting enterprise. After the initial phase, getting finance is easier. Good companies can always raise money from the venture-capital market, says Seppo Mäkinen of BioFund.

For now, biotechnology in Finland is young and overwhelmingly privately owned. Only two companies have gone public: Bionx Implants, which makes surgical implants, is listed on the Nasdaq exchange, and BioTie Therapies is listed on the Helsinki Stock Exchange. Fibrogen Europe, a developer of collagen-based products with a US parent company (FibroGen, South San Francisco, California), will most likely be the next to go public, probably on the Helsinki Stock Exchange. Recently, Ark Therapeutics, which has a parent company in London, announced its intention to list on the London Stock Exchange. But several firms have products on or close to the market, and Finnish biotechnology seems determined to make Scandinavian biotechnology into one of Europe's hot topics. ■

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This article is an updated version of a feature published in *Nature Biotechnology* (20, 437–440; 2002).



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